Childhood smoking is an independent risk factor for obstructive airways disease in women

B D Patel, R N Luben, A A Welch, S A Bingham, K-T Khaw, N E Day, D A Lomas, N J Wareham

Objective: To assess whether starting to smoke in childhood increases the risk of obstructive airways disease (OAD) in adult life.

Methods: A retrospective cohort analysis was undertaken of 12 504 current and ex-smokers in the EPIC-Norfolk cohort. The main exposure was starting to smoke during childhood (age <16 years). Three definitions of OAD were used: doctor diagnosed asthma, doctor diagnosed bronchitis/emphysema, and ‘any OAD’ (doctor diagnosed asthma or bronchitis/emphysema, or taking medication used in the treatment of OAD).

Results: Childhood smokers had significantly more pack years of exposure and poorer lung function than subjects who started to smoke in adulthood (≥16 years). Compared with starting in adulthood, starting to smoke in childhood was associated with a greater risk of bronchitis/emphysema in female smokers (OR 1.79, 95% CI 1.25 to 2.56) and ex-smokers of both sexes (OR 1.29, 95% CI 1.07 to 1.55 in men and OR 1.40, 95% CI 1.05 to 1.85 in women), and of ‘any OAD’ in female smokers (OR 1.72, 95% CI 1.24 to 2.38) and male and female ex-smokers (OR 1.20, 95% CI 1.03 to 1.40 in men and 1.34, 95% CI 1.07 to 1.57 in women). After adjustment for pack years, childhood smoking was associated with poorer lung function (FEV₁ 92.3% predicted in adult smokers and 89.5% in childhood smokers, p = 0.03) and a greater risk of bronchitis/emphysema (adjusted OR 1.55, 95% CI 1.08 to 2.24) and for ‘any OAD’ (OR 1.54, 95% CI 1.10 to 2.13) in female smokers but not in male and female ex-smokers.

Conclusion: Starting to smoke in childhood is associated with an increased risk of airways disease because of the extra pack years smoked. In women, childhood smoking is itself an independent risk factor for the development of airways disease.

Over the past 25 years the prevalence of smoking has remained stable in English children aged 11–15 years at a time when smoking rates have fallen in adults. Similar trends have been reported in other European countries and the USA, and in all cases the prevalence of smoking in young girls is equal to or greater than that in boys. Although cigarette smoking is the major environmental risk factor for the development of chronic obstructive pulmonary disease (COPD), only about 15% of smokers develop significant airflow obstruction. The development of COPD in a minority of smokers has been attributed to a greatly accelerated rate of decline of forced expiratory volume in 1 second (FEV₁) in ‘susceptible smokers’. Even without this additional susceptibility, smokers who enter adult life with a low FEV₁ may be at risk of developing airflow obstruction as a result of the modestly increased rate of decline in FEV₁ observed in the majority of smokers.

A substantial proportion of adult smokers start to smoke in childhood. Childhood smokers are more likely to continue smoking than individuals who start smoking in later life, and therefore may be expected to have a greater risk of developing COPD as a result of their greater cumulative tobacco consumption. It has been shown that children who smoke experience more respiratory symptoms and have poorer lung function than their non-smoking peers. However, it is not clear whether the reduced lung growth experienced by childhood smokers is an independent risk factor for the development of obstructive airways disease in later life. We addressed these questions using data from the Norfolk arm of the European Prospective Investigation of Cancer (EPIC-Norfolk). In a retrospective analysis we assessed the independent effects of childhood smoking and cumulative tobacco consumption on the risk of airways disease in adult life.

METHODS

The EPIC-Norfolk cohort is a population based cohort of men and women aged 45–75 years. The primary objective of the EPIC-Norfolk cohort is to prospectively assess the association of diet and other lifestyle exposures with the development of chronic disease. The individuals in the study were recruited from 35 general practices in and around the city of Norwich. A detailed description of the recruitment, operation and characteristics of the cohort is published elsewhere.

Between 1993 and 1998, 24 842 people (13 444 of whom were current or ex-smokers) attended for a health check at which anthropometric measurements were made and spirometric tests performed. Spirometric tests were conducted by a nurse trained in the technique using a hand held electronic turbine spirometer (Micro Medical Instruments, Rochester, UK). Two standing measurements were made and the higher of the two values of FEV₁ was used.

Smoking status was obtained from a health and lifestyle questionnaire by the response to the question: “Have you ever smoked as much as one cigarette per day for a year?” Current smokers were identified by a positive response to the question: “Do you smoke cigarettes now?” Individuals who responded positively to the first question but negatively to the second question were classified as ex-smokers. Pack years smoked were calculated from the reported age of starting, age of quitting, and the number of cigarettes smoked at age 20, 30, 40, 50 and at the time of the study. The algorithm used to calculate total pack years took into account periods of abstinence. The average number smoked per day was
Childhood smoking and OAD

Cox regression analysis was used to assess the effects of smoking status (current and ex-smokers) using two methods. Firstly, for each of the three definitions of OAD we estimated the stratum specific risk ratio for childhood smokers relative to those who started in adulthood. Secondly, we assessed the effect of childhood smoking on FEV₁ percent predicted. Predicted values of FEV₁ were calculated independently for each sex using regression coefficients derived for height and age on FEV₁ in 3238 men and 6467 women in the EPIC-Norfolk cohort who were lifetime non-smokers without OAD. Differences in proportions were compared using a χ² test. For continuous variables the differences in means between groups were compared using the Student’s t test, Kruskal-Wallis test, or analysis of variance (ANOVA) as appropriate. Multiple logistic regression models were used to estimate odds ratios with potential confounding variables included as covariates. Effect modification of the association by sex was assessed in pooled analyses of men and women by the inclusion of an interaction term between sex and childhood smoking.

RESULTS

The age at which subjects first started to smoke was available for 12 504 (93%) current and ex-smokers who performed spirometric tests (table 1). More than twice as many men than women reported starting to smoke in childhood (37.2% male smokers v 16.2% female smokers, p ≤ 0.001; 27.2% male ex-smokers v 12.0% female ex-smokers, p ≤ 0.001). In all cases childhood smokers had significantly more cumulative pack years of exposure due to a combination of heavier smoking.

Table 1  Characteristics of current and ex-smokers by sex and age of starting to smoke

<table>
<thead>
<tr>
<th></th>
<th>Male smokers (n = 1294)</th>
<th>Male ex-smokers (n = 5792)</th>
<th>Female smokers (n = 1416)</th>
<th>Female ex-smokers (n = 4002)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.8 (8.9)</td>
<td>57.6 (8.9)</td>
<td>60.4 (9.1)</td>
<td>62.8 (9.2)</td>
</tr>
<tr>
<td>Percentage (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>37.2 (481)</td>
<td>62.8 (813)</td>
<td>16.2 (230)</td>
<td>83.8 (1186)</td>
</tr>
<tr>
<td>Childhood Adulthood</td>
<td>27.2 (1575)</td>
<td>72.8 (4217)</td>
<td>53.7 (81)</td>
<td>56.7 (87.7)</td>
</tr>
<tr>
<td>Adulthood</td>
<td></td>
<td></td>
<td>61.5 (9.2)</td>
<td>61.5 (9.2)</td>
</tr>
<tr>
<td>Age started smoking years</td>
<td>13.9 (1.6)</td>
<td>18.4 (4.0)</td>
<td>14.1 (1.3)</td>
<td>19.8 (3.2)</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>19.2 (7.1)</td>
<td>16.3 (7.1)</td>
<td>20.3 (9.9)</td>
<td>15.9 (9.2)</td>
</tr>
<tr>
<td>Years of smoking</td>
<td>42.9 (9.2)</td>
<td>39.2 (9.4)</td>
<td>23.2 (15.8)</td>
<td>19.2 (14.2)</td>
</tr>
<tr>
<td>Pack years</td>
<td>38.1 (17.8)</td>
<td>38.2 (15.5)</td>
<td>26.1 (20.3)</td>
<td>16.6 (16.1)</td>
</tr>
<tr>
<td>Asthma, % (n)</td>
<td>5.4 (26)</td>
<td>6.8 (55)</td>
<td>8.8 (138)</td>
<td>7.9 (334)</td>
</tr>
<tr>
<td>Bronchitis/ emphysema, % (n)</td>
<td>11.5 (55)</td>
<td>10.5 (85)</td>
<td>11.6 (182)</td>
<td>9.2 (389)</td>
</tr>
<tr>
<td>“Any OAD”, % (n)</td>
<td>16.3 (78)</td>
<td>14.6 (199)</td>
<td>17.9 (281)</td>
<td>15.3 (644)</td>
</tr>
</tbody>
</table>

Figures are mean (SD) or % (n).

Cigarettes per day = the mean number of cigarettes smoked per day while an active smoker.

“Any OAD” is defined as the presence of doctor diagnosed asthma or doctor diagnosed bronchitis/emphysema, or self-reported taking of medication for airways disease.

*p < 0.05, tp < 0.01, tp < 0.001 for the difference within smoking categories between those who started to smoke in childhood (age < 16 years) and those who started in adulthood (age ≥ 16 years).

Statistical analysis

Cox regression analysis was used to assess the effects of starting to smoke in childhood on the subsequent risk of quitting. The association between childhood smoking and airways disease was assessed independently in men and women stratified by smoking status (current and ex-smokers) using two methods. Firstly, for each of the three definitions of OAD we estimated the stratum specific risk ratio for childhood smokers relative to those who started in adulthood. Secondly, we assessed the effect of childhood smoking on FEV₁ percent predicted. Predicted values of FEV₁ were calculated independently for each sex using regression coefficients derived for height and age on FEV₁ in 3238 men and 6467 women in the EPIC-Norfolk cohort who were lifetime non-smokers without OAD. Differences in proportions were compared using a χ² test. For continuous variables the differences in means between groups were compared using the Student’s t test, Kruskal-Wallis test, or analysis of variance (ANOVA) as appropriate. Multiple logistic regression models were used to estimate odds ratios with potential confounding variables included as covariates. Effect modification of the association by sex was assessed in pooled analyses of men and women by the inclusion of an interaction term between sex and childhood smoking.
smoking (more cigarettes consumed a day) and a greater duration of smoking. The proportion of ever smokers who subsequently quit was greater in men than in women (81.3% vs 73.8%, \( p < 0.001 \)) but, within each sex, childhood smokers were less likely to quit (fig 1). The hazard ratio (HR) for quitting in those who started smoking in adulthood relative to childhood smokers was 1.54 (CI 1.44 to 1.63, \( p < 0.001 \)) in men and 1.49 (CI 1.31 to 1.59, \( p < 0.001 \)) in women. The likelihood of quitting showed a significant trend across social class in both sexes with those in social class 5 being less likely to quit smoking (\( p < 0.001 \), test for trend within each sex). However, after adjusting for smoking related to childhood smoking in adulthood, although the difference was not statistically significant. Moreover, neither exposure was significant as a covariate after adjustment for pack years.

The results of these analyses are summarised in table 3. After adjusting for pack years smoked, the excess risk for chronic bronchitis/emphysema and “any OAD” associated with smoking in childhood was no longer significant in male and female ex-smokers. Thus, in these individuals the increased risk of OAD associated with smoking in childhood is explained by the extra pack years smoked. In women who continued to smoke, starting to smoke in childhood remained an independent risk factor for the development of bronchitis/emphysema and “any OAD”, even after adjustment for the extra pack years of smoking. Additional adjustment for number of cigarettes smoked per day and years of smoking did not affect the association with childhood smoking in these women. Moreover, neither exposure was significant as a covariate after adjustment for pack years.

### Table 2: Association between tobacco consumption and risk of physician diagnosed airways disease

<table>
<thead>
<tr>
<th>Smoking exposure</th>
<th>Asthma OR (95% CI)</th>
<th>Bronchitis/emphysema OR (95% CI)</th>
<th>“Any OAD” OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Per 10 cigarettes/day</td>
<td>1.02 (0.95 to 1.09)</td>
<td>1.20* (1.13 to 1.28)</td>
<td>1.00 (0.90 to 1.11)</td>
</tr>
<tr>
<td>Per 10 years of smoking</td>
<td>1.00 (0.96 to 1.04)</td>
<td>1.15* (1.11 to 1.20)</td>
<td>1.06 (1.00 to 1.11)</td>
</tr>
<tr>
<td>Per 10 pack years smoked</td>
<td>1.01 (0.98 to 1.05)</td>
<td>1.16* (1.13 to 1.20)</td>
<td>1.14* (1.07 to 1.21)</td>
</tr>
</tbody>
</table>

* \( p < 0.0001 \). The reference categories were less than 10 cigarettes per day, less than 10 years of smoking, and less than 10 pack years of cumulative smoking. The unadjusted odds ratio is the univariate association of each smoking exposure. The adjusted odds ratio is the mutually adjusted odds ratio.

### Table 3: Odds ratios for the presence of airways disease in childhood smokers by sex and smoking status

<table>
<thead>
<tr>
<th>Disease</th>
<th>Model</th>
<th>Men smokers</th>
<th>Men ex-smokers</th>
<th>Women smokers</th>
<th>Women ex-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Unadjusted</td>
<td>0.79 (0.49 to 1.27)</td>
<td>1.11 (0.91 to 1.37)</td>
<td>1.63 (1.02 to 2.59)</td>
<td>1.27 (0.95 to 1.69)</td>
</tr>
<tr>
<td></td>
<td>Adjusted for pack years</td>
<td>0.81 (0.49 to 1.33)</td>
<td>1.06 (0.86 to 1.32)</td>
<td>1.59 (0.99 to 2.54)</td>
<td>1.19 (0.88 to 1.60)</td>
</tr>
<tr>
<td>Bronchitis/emphysema</td>
<td>Unadjusted</td>
<td>1.11 (0.78 to 1.60)</td>
<td>1.29 (1.07 to 1.55)</td>
<td>1.79 (1.25 to 2.56)</td>
<td>1.40 (1.05 to 1.85)</td>
</tr>
<tr>
<td></td>
<td>Adjusted for pack years</td>
<td>0.96 (0.66 to 1.39)</td>
<td>1.12 (0.92 to 1.36)</td>
<td>1.55 (1.08 to 2.24)</td>
<td>1.22 (0.92 to 1.63)</td>
</tr>
<tr>
<td>“Any OAD”</td>
<td>Unadjusted</td>
<td>1.14 (0.83 to 1.55)</td>
<td>1.20 (1.03 to 1.40)</td>
<td>1.72 (1.24 to 2.38)</td>
<td>1.34 (1.07 to 1.57)</td>
</tr>
<tr>
<td></td>
<td>Adjusted for pack years</td>
<td>0.99 (0.72 to 1.37)</td>
<td>1.08 (0.92 to 1.27)</td>
<td>1.54 (1.10 to 2.13)</td>
<td>1.24 (0.98 to 1.56)</td>
</tr>
</tbody>
</table>

Data are shown as odds ratios (95% CI) for childhood smokers relative to those who started smoking in adulthood within each smoking category.

\( \* p < 0.05 \); \( \ddagger p < 0.02 \); \( \dagger p < 0.008 \); \( * p < 0.001 \).
difference in percentage predicted FEV\(_1\) in male current smokers and male and female ex-smokers. However, even after adjustment for pack years smoked, the percentage predicted FEV\(_1\) remained significantly lower in female current smokers who started smoking in childhood (adjusted FEV\(_1\) 92.3\% predicted in adult smokers and 89.5\% in childhood smokers, \(p = 0.03\)).

**DISCUSSION**

The prevalence of smoking in children age 13–15 years is as high as 40\% in some countries.\(^{26}\) Our results show that, in addition to being more likely to continue smoking, childhood smokers have a greater risk of OAD and a lower FEV\(_1\) in adult life than those who start smoking in adulthood. In male and female ex-smokers the excess risk of lung disease is explained by the greater number of pack years smoked. In women who continue to smoke the increased risk of airways disease and reduction in FEV\(_1\) associated with childhood smoking is in addition to the increased number of pack years. Exposure to cigarette smoke during childhood is itself therefore an independent risk factor for the development of airways disease in these women.

It has been suggested that women who smoke may be at greater risk of developing COPD than men,\(^{21}\) and studies in adults suggest that women may be more susceptible to the effects of both active and passive smoking. Differences between men and women in the effects of smoking on pulmonary function and respiratory symptoms have also been described in young smokers.\(^{14,18,22}\) In a recent longitudinal study the adverse effects of smoking on rate of lung growth were significantly greater in young female smokers than in male smokers. Moreover, whereas non-smoking females had a plateau in the FEV\(_1\) at age 16–17, female smokers showed a decline in FEV\(_1\) at this age.\(^{15}\) Our findings suggest that these effects of early life smoking persist into adult life in women who continue to smoke, and may contribute to an increased risk of COPD in female smokers.

The fact that we did not see this effect in women who were ex-smokers may be due to a number of factors. Ex-smokers are a heterogeneous group who may have stopped smoking for a variety of reasons—including social, cultural and health factors such as the onset of respiratory symptoms. Moreover, smoking cessation in early to mid life may be associated with some recovery in lung function, suggesting compensation for the excess loss in FEV\(_1\) that occurred during the period of smoking.\(^{23,24}\)

The normal development of lung function in childhood and adult life has been described in a number of studies.\(^{17,23,25,26}\) In healthy non-smokers the FEV\(_1\) increases during childhood and early adult life. This is followed by a plateau phase after which there is a decline with increasing age.\(^{23,25-27}\) The finding that childhood smoking is an independent risk factor for OAD in women but not in men could be explained by differences in lung development between the sexes. Women reach their maximum FEV\(_1\) at an earlier age\(^{27}\) and have a shorter plateau phase than men and an earlier onset of decline in FEV\(_1\).\(^{25,27}\) In this analysis we defined childhood smokers as individuals who started smoking before the age of 16 years. However, the stage of lung maturation at this age differs between the sexes. In females it corresponds to the start of the plateau phase while in males the lung volume continues to increase into the third decade of life.\(^{28}\) In stratifying male smokers by age 16 years we may therefore have missed an independent effect of early life smoking. We have subsequently repeated the analysis comparing men who started to smoke before and after age 25. This analysis did not show an independent effect of smoking below this age. However, as less than 4\% of men in this cohort started smoking after the age of 25, the analysis may have had inadequate power to detect a significant effect.

The prevalence of doctor diagnosed chronic bronchitis/ emphysema was lower in male smokers (10.8\%) than in female smokers (14.7\%). Although this raises the possibility of diagnostic bias, it could reflect a higher prevalence of respiratory symptoms in female than in male smokers as has been previously reported.\(^{29}\) An alternative explanation for this finding would be an over-representation of healthy smokers among men in the EPIC-Norfolk cohort. This seems unlikely as there was no significant difference in the prevalence of asthma between male smokers (6.3\%) and female smokers (7.9\%). Moreover, FEV\(_1\) percent predicted was significantly lower in male smokers (86.1\%) than in female smokers (90.3\%, \(p < 0.001\)).

The association between smoking and airways disease was better explained by cumulative pack years of smoking than by duration or number smoked per day. In assessing the risk of childhood smoking we adjusted for the major confounding factor—pack years smoked. Although we adjusted for social class, we were unable to adjust for occupational exposure to dust and fumes which have been associated with an increased decline in FEV\(_1\)\(^{30,31}\) However, the East Anglia region of the UK is not heavily industrialised and does not have a high prevalence of occupational lung disease. We were also unable to adjust for the effects of parental social class or for parental smoking which is itself a risk factor for smoking in childhood.\(^{35,32}\) Moreover, early life exposure to environmental tobacco smoke has been associated with reduced pulmonary function. However, the effect of this is small.\(^{17,33}\) Data were also unavailable on childhood respiratory tract infections which may be associated with an increased risk of adult obstructive airways disease.\(^{34}\)

The results of this study give considerable cause for concern as smoking remains prevalent among school children in many societies. Government spending in the UK on the prevention of smoking in young people constitutes a small fraction of the estimated revenue generated from childhood smoking and is tiny in relation to expenditure by tobacco companies on promotional campaigns.\(^{35}\) Our findings suggest that there should be a greater focus of public health policy on addressing smoking in school children. For example, although several surveys have found that most young smokers wish to stop,\(^{3,20,32}\) there has been little effort into the efficacy of cessation strategies in this age group.\(^{5,15}\) It has been suggested that it is inefficient to focus limited resources on tackling smoking in children since they constitute only a small percentage of all smokers.\(^{36,37}\) The results presented here are at odds with this view. Children who smoke are more likely to become persistent adult smokers and, either because of their greater cumulative tobacco consumption or the effects of smoking on lung development, are at greater risk of developing OAD.
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REFERENCES

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